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Review article

Mechanical chest compression for out of hospital cardiac arrest: Systematic review and meta-analysis[☆]



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ABSTRACT

Aim: To summarise the evidence from randomised controlled trials of mechanical chest compression devices used during resuscitation after out of hospital cardiac arrest.

Methods: Systematic review of studies evaluating the effectiveness of mechanical chest compression. We included randomised controlled trials or cluster randomised trials that compared mechanical chest compression (using any device) with manual chest compression for adult patients following out-of-hospital cardiac arrest. Outcome measures were return of spontaneous circulation, survival of event, overall survival, survival with good neurological outcome. Results were combined using random-effects meta-analysis.

Data sources: Studies were identified by searches of electronic databases, reference lists of other studies and review articles.

Results: Five trials were included, of which three evaluated the LUCAS or LUCAS-2 device and two evaluated the AutoPulse device. The results did not show an advantage to the use of mechanical chest compression devices for survival to discharge/30 days (average OR 0.89, 95% CI 0.77, 1.02) and survival with good neurological outcome (average OR 0.76, 95% CI 0.53, 1.11).

Conclusions: Existing studies do not suggest that mechanical chest compression devices are superior to manual chest compression, when used during resuscitation after out of hospital cardiac arrest.

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1. Introduction

Out of hospital cardiac arrest is a major cause of death and morbidity.¹ Survival rates are low; in the UK, only around 7% of patients in whom resuscitation is attempted, survive to discharge from hospital.² A key factor that improves survival is good quality cardiopulmonary resuscitation (CPR).^{3,4}

The quality of CPR delivered at out-of-hospital cardiac arrest is often sub-optimal.⁵ Fatigue and the need to deliver multiple tasks on arrival at a cardiac arrest likely limit the quality of CPR that

paramedics can provide. Mechanical chest compression devices provide compressions of standard depth and frequency for prolonged periods without any decline in quality and remove the need for paramedics to provide chest compressions manually, enabling them to concentrate on other aspects of patient care.⁶

Several different types of mechanical chest compression device have been proposed, but the main technologies are piston devices and load-distributing bands. Piston devices such as LUCAS-2 (Jolife AB, Sweden) use a piston mounted on a frame that fits around the patient's chest. The piston is driven up and down by a power source such as compressed air or an electric motor, compressing the chest in a similar way to manual chest compressions. Load-distributing band devices, such as AutoPulse (Zoll Medical Corporation, Chelmsford, MA), work in a different way. They consist of a wide band that fits around the chest, whose circumference is alternately shortened and lengthened, providing rhythmic chest compressions.

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Three large randomised controlled trials that compared mechanical with manual chest compression, and evaluated their effects on clinically important outcomes, have recently been reported, but not yet included in systematic reviews. The aim of this paper is to combine, where appropriate, the results from randomised trials, to estimate the effects on important outcomes (especially survival and survival with good neurological outcome) of mechanical chest compression devices used to provide chest compressions for adult patients after out of hospital cardiac arrest.

2. Methods

Studies were eligible for inclusion if they were individually randomised or cluster randomised trials that compared the use of a mechanical chest compression device with standard manual chest compression in adult patients following out of hospital cardiac arrest. There was no restriction of eligibility based on language of publication. Quasi-randomised trials, for example, those randomised by birth date or days of the week, were excluded. Studies were not included in analyses if they reported insufficient information to allow assessment of their risk of bias. Screening, decisions about inclusion and data extraction were performed by one author and checked by a second author. The review protocol was not pre-registered or published.

We searched electronic resources (Medline, EMBASE and the Cochrane Central register from 1990 to February 2015) and the reference lists of studies and review articles (last search February 2015). We based our search strategies on that published by the Cochrane review of mechanical chest compression devices,⁷ which used a combination of search terms to describe the condition (cardiac arrest), the intervention (mechanical compression devices) and the study design (randomised controlled trials).

For each eligible study, we extracted information about the study's population and methodology, and the following outcomes; return of spontaneous circulation (ROSC); survived event (sustained ROSC until handover to a hospital emergency department); survival to hospital discharge or 30 days; and survival with good neurological outcome. Good neurological outcome was defined as either a Cerebral Performance Category (CPC) score of 1 or 2, or Modified Rankin Scale (mRS) score of between 0 and 3.⁸ Where studies presented a treatment effect estimate adjusted for important covariates (e.g. clustering, initial rhythm, bystander CPR, EMS response time, age) we used this estimate in meta-analyses in preference to unadjusted results.

We used the Cochrane Risk of Bias tool to assess studies' risk of bias. This assesses seven domains; generation of random allocation sequence, allocation concealment, blinding of participants and study personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. For each study, we assessed the methods used to address each potential source of bias, and summarised them in tabular form. We did not produce an overall bias risk judgement or score, but assessed each domain separately.

We combined studies using the Review Manager (RevMan) software version 5.3. Because there may be differences in treatment effect between trials, especially those using different devices, we used a random-effects model. We used the generic inverse variance method in RevMan to estimate the average treatment effect (odds ratio) for each outcome, and the uncertainty around it, measured by the 95% confidence interval. We also calculated 95% prediction intervals,⁹ to estimate the range of plausible treatment effects. We quantified heterogeneity in each analysis by the tau-squared and *I*-squared statistics. Studies were subgrouped by the type of mechanical compression device used, as different devices operate in different ways and hence could have different treatment

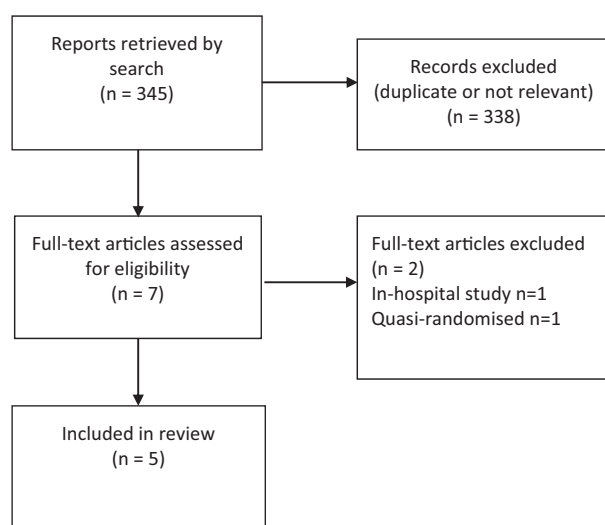


Fig. 1. Flow chart of studies.

effects. Our primary analysis compared mechanical compression with manual compression, and we performed a subgroup analysis by type of device, to explore whether there was any evidence that treatment effects differed between devices.

Some of the included trials presented several results using different adjustments for covariates and design elements. We performed sensitivity analyses to explore the effects of using differently adjusted results for these trials. In addition, PARAMEDIC presented CACE (complier average causal effect) estimates, to estimate the treatment effect in the presence of non-compliance.^{10,11} We performed additional sensitivity analyses to explore the effects of using these estimates.

3. Results

The search located five eligible studies^{12–16} (Fig. 1). Two trials evaluated the AutoPulse device, and three evaluated the LUCAS device. Two of the studies used a cluster randomised design, one (PARAMEDIC) randomising by ambulance service vehicles, and the other (ASPIRE) using ambulance stations or groups of stations as the clusters; this study also incorporated crossovers at prespecified points between the intervention and control groups. The other three studies employed individual randomisation, using sealed envelopes or cards carried with the device, which were accessed by the paramedic at the time of the resuscitation attempt. Study characteristics and risk of bias are summarised in Table 1.

There were a number of differences between the studies in addition to the chest compression device used, which may have caused differences in treatment effects and hence introduce heterogeneity into the meta-analyses. In two studies the LUCAS device was used as part of a modified treatment algorithm,^{13,14} whereas in the third LUCAS study mechanical chest compression was simply used to replace manual compression in the standard algorithm.¹⁶ One of the trials of AutoPulse conducted extensive training to optimise the quality of manual CPR that was provided to the control group¹⁷; in contrast other trials did not provide extra training but the control group received CPR as it would be provided in standard clinical practice.

The randomisation methods of the studies appeared to be adequate, although four studies did not provide any information on the generation of the random allocation sequence. One concern with individual randomisation was that it would be possible for ambulance staff to open randomisation envelopes early and subvert the randomisation scheme. No studies reported any problems with

Table 1
Characteristics of studies and bias risk assessments.

Study	Unit of randomisation	Study setting	Recruitment period	Intervention	Number of participants	Sequence generation	Allocation concealment	Blinding; patients and clinicians	Blinding; outcome assessment	Percentage of participants with missing data for each outcome	Selective reporting	Other sources of bias
ASPIRE 2006	Cluster – crossover at predetermined intervals	USA/Canada	2004–2005	AutoPulse	767 51 clusters (EMS stations or groups of stations)	No information	Not concealed; ambulance staff aware of intervention	Not blinded	Unclear	Survival: 0% Survival with CPC 1–2: 0.7% Primary analysis included 767 “primary” cases, 304 “nonprimary” cases and 306 with exclusion criteria excluded	No evidence	Participants with missing CPC were 8.3% of survivors
Smekal 2011	Patient	Sweden	2005–2007	LUCAS	148	No information	Sealed randomisation letter carried with device, opened at time of randomisation	Not blinded	Unclear	Survival: 0.7% ROSC: 1.4% Survived event: 0.7%	No evidence	
LINC 2014	Patient	Sweden, UK, Netherlands	2008–2012	LUCAS/LUCAS-2	2589	No information	Sealed opaque envelopes carried in ambulance, opened at time of randomisation	Not blinded	Unclear	Survival: 1.1% ROSC: 0.1% Survived event: 0% Survival with CPC 1–2: 1.1%	No evidence	
CIRC 2014	Patient	Austria, Netherlands, USA	2009–2011	AutoPulse	4231	No information	Sealed randomisation cards opened when indication for CPR was found	Not blinded	“Not always blinded”	Survival: 0.3% ROSC: 0% Survival with mRS 0–3: 2.8% 522 participants satisfying exclusion criteria excluded post-randomisation. Primary analysis excluded participants in “run-in” phase and those recruited in early part of trial when battery issues led to poor compliance.	No evidence	Participants with missing mRS were 27.7% of survivors
PARAMEDIC 2015	Cluster	UK	2010–2013	LUCAS-2	4471 418 clusters (vehicles)	Computer-generated stratified by station and vehicle type	Not concealed; ambulance staff aware of intervention	Not blinded	Survival from routine data. Neurological status assessment blinded	Survival: 0% ROSC: 3.1% Survived event: 4.7% Survival with CPC 1–2: 0.2%	No evidence	Participants with missing CPC were 2.5% of survivors

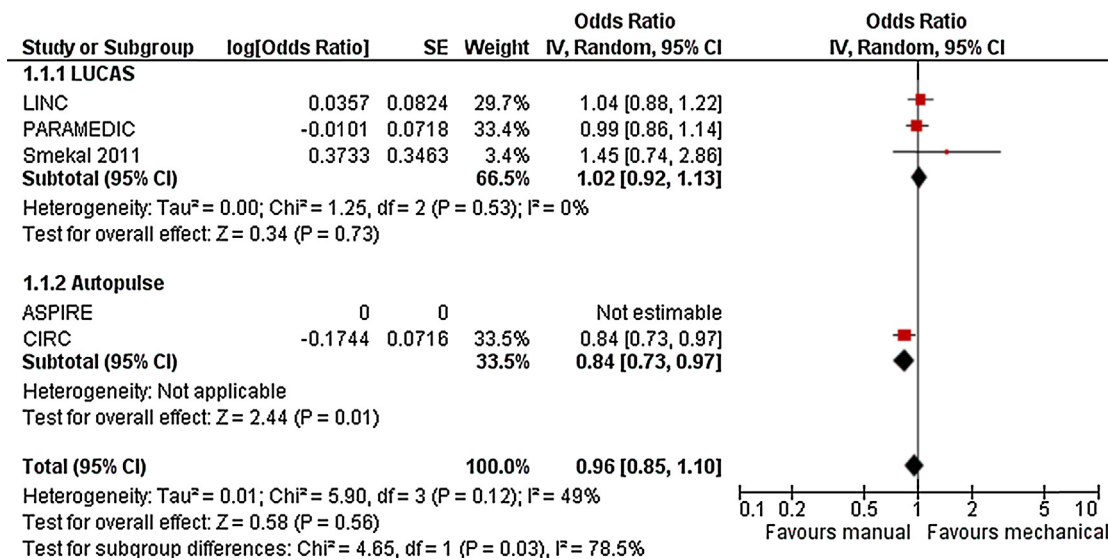


Fig. 2. Return of spontaneous circulation.

individual randomisation procedures, such as missing randomisation cards that could not be accounted for (which might indicate that crews had selected the intervention), or large numbers of eligible patients that were not recruited (which might suggest that the crew felt that the randomised allocation would not be good for the patient).

Blinding of clinicians providing care was clearly not possible, and participants who survived may also have been aware of which allocation they had received. For example, use of the LUCAS device may leave characteristic marks on the patient's chest. Assessment of survival outcomes was unlikely to have been affected by whether or not the people assessing the outcome were blinded. One study stated that personnel assessing neurological status (CPC or mRS) were blinded; in other studies this was unclear. It is conceivable that knowledge of treatment allocations could influence assessments of neurological status; if assessors had strong views on the effectiveness of the intervention being tested, they may have adjusted their threshold for allocating a patient to an mRS or CPC category. We cannot exclude this potential bias in studies where outcome assessment was not blinded.

In all trials, the proportion of missing outcome data was low, when measured as a percentage of all study participants. However, in some trials, there was potentially bias due to missing data in the assessment of neurologically intact survival. This was because the missing data were concentrated among survivors; for example, in CIRC, although only 2.8% of participants had missing mRS data, they represented 27.7% of survivors. The populations included varied between trials. In ASPIRE, results were presented for a prespecified "primary" population (patients who were in cardiac arrest at the time of EMS arrival and whose cardiac arrest was considered to be of cardiac origin). Patients who fulfilled exclusion criteria were treated according to trial allocation but subsequently excluded (in order not to introduce delays to treatment), but 304 "nonprimary" cases were also excluded from the main results. In CIRC, there were also 522 post-randomisation exclusions of patients fulfilling exclusion criteria. However, this trial also excluded patients recruited in a prespecified run-in phase, an unspecified number of patients recruited early in the trial (after the run-in period) when compliance with AutoPulse was found to be poor due to battery issues, and data from one site for a three-month period when that site was non-compliant with the study protocol (number not stated).

The CIRC trial used a group-sequential design with predefined stopping boundaries for superiority, inferiority and equivalence

(double triangular test).^{17,18} The trial report presented treatment effect estimates adjusted for clinical covariates for all outcomes, but additionally adjusted the primary outcome (survival to hospital discharge) for the sequence of interim analyses. In this review we have used the results adjusted for covariates but not for the interim analyses, because these are consistent and based on the data rather than the decision making process. We explored the effect of the adjustment of the primary outcome for interim analyses with a sensitivity analysis.

The meta-analyses (Figs. 2–5) do not suggest an advantage to mechanical chest compression, using either device, for any of the outcomes. Confidence intervals and prediction intervals were wide, reflecting the low incidence of favourable outcomes after out-of-hospital cardiac arrest, and consequent imprecision of treatment effect estimates.

For ROSC (Fig. 2), although there was no evidence of an overall difference between mechanical and manual chest compression (average OR 0.96, 95% CI 0.85, 1.10, 95% prediction interval 0.66, 1.41), there was some evidence that the effects of LUCAS and AutoPulse were different (I^2 for subgroup differences 78.5%). There was data from only one AutoPulse trial, but that suggested a lower proportion achieving ROSC in the mechanical chest compression group.

Survival of event was only reported by trials that used LUCAS (Fig. 3); the results were consistent across trials and suggested no advantage to mechanical chest compression devices (OR 0.95, 95% CI 0.85, 1.07, 95% prediction interval 0.45, 2.00).

The analysis of survival to discharge or 30 days (Fig. 4), again suggested no advantage to mechanical chest compression (OR 0.89, 95% CI 0.77, 1.02, 95% prediction interval 0.71, 1.12). The point estimate was in the direction of favouring manual chest compression, and the upper 95% confidence limit was only just greater than 1. There was no evidence of heterogeneity of treatment effects. Sensitivity analysis using the estimate for CIRC adjusted for interim analyses as well as covariates did not make a major difference to the overall average treatment effect (OR 0.94, 95% CI 0.79, 1.11, 95% prediction interval 0.62, 1.43). Similarly, sensitivity analyses using the CACE estimates for PARAMEDIC did not make a substantial difference to the overall result.

Results for survival with good neurological outcome (Fig. 5) were more heterogeneous than for other outcomes (I^2 68%). This was not due to differences between LUCAS and AutoPulse, which were small (I^2 for subgroup differences 11%), but to inconsistency

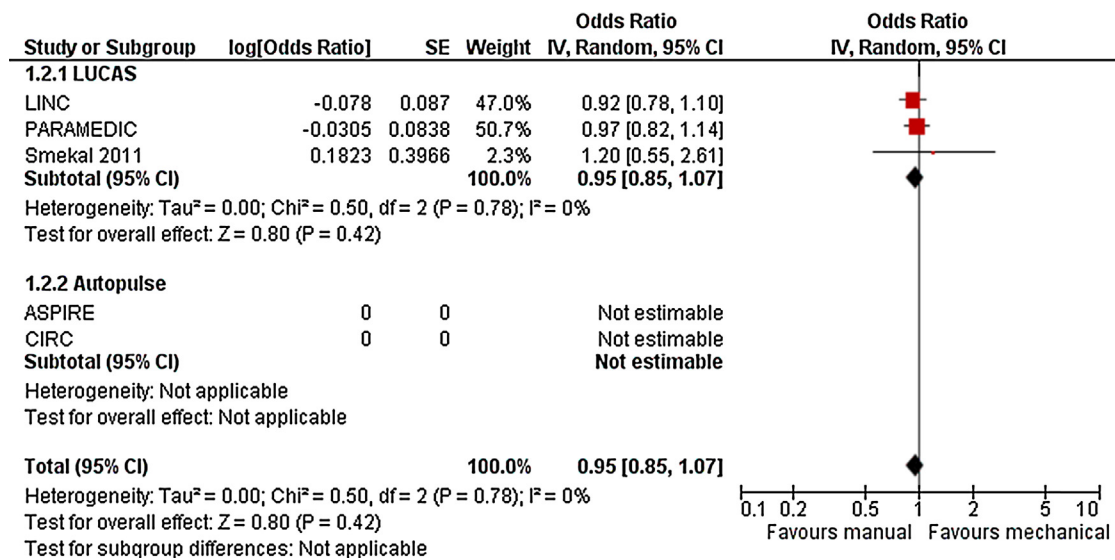


Fig. 3. Survived event (i.e. sustained ROSC to handover to hospital emergency department).

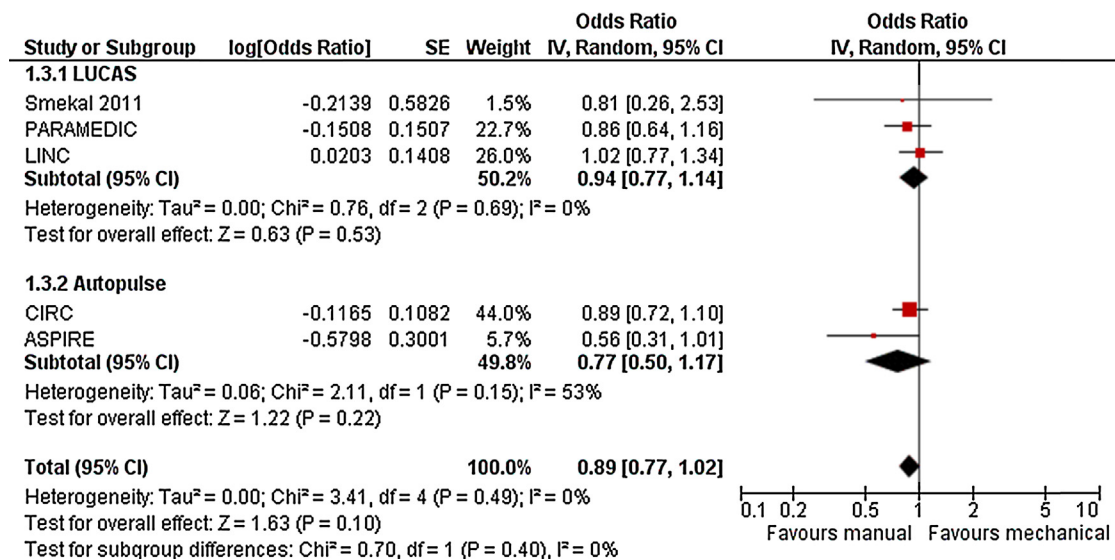


Fig. 4. Survival to discharge from hospital or 30 days.

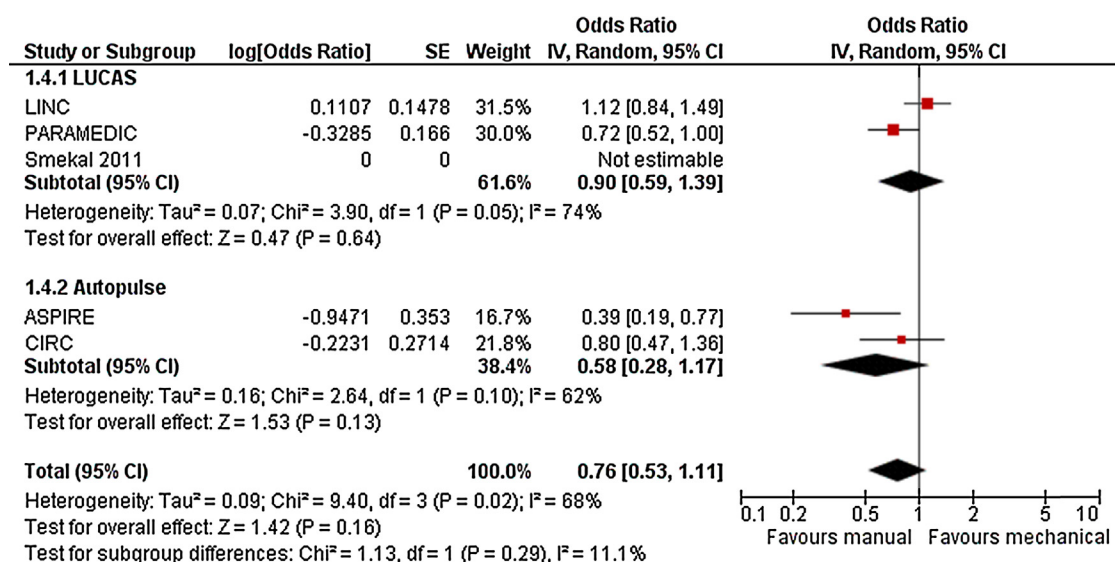


Fig. 5. Survival with CPC 1–2 or mRS 0–3.

between the results of the two trials of each device. Reasons for the inconsistency were unclear. Overall, there was no evidence that the average treatment effect favoured mechanical chest compression, but the 95% prediction interval was very wide (OR 0.76, 95% CI 0.53, 1.11, 95% prediction interval 0.17, 3.49).

4. Discussion

Five randomised trials, involving over 10,000 participants, were included. The meta-analyses found no evidence of benefit with the use of mechanical chest compression devices. Results for survival with good neurological outcome were heterogeneous, and both confidence intervals and prediction intervals were wide, and do not rule out benefit in some trials. Because of the inclusion of recent large trials in this review, our conclusions can be firmer than those of the most recent update of the Cochrane review.⁷ They also differ from those of another recent review and meta-analysis,¹⁹ which found, mainly from observational evidence, an improvement in the odds of ROSC with mechanical chest compression.

The trials recruited unselected populations of patients typical of clinical practice in the geographical areas in which they were conducted. Despite the large size of many of the trials included in the review, confidence intervals around the combined treatment effect estimates were relatively wide, because of the low survival rate from out of hospital cardiac arrest. The methodological quality of the included studies was generally good. Secure methods of randomisation were used, and for most outcomes there were few missing data. Trials using a cluster randomised design were unable to conceal allocations in advance of assignment, and ambulance crews would have been aware of the allocation. This could have led to inclusion bias, in two ways. First, patients might not be reported to the trial if it was felt that they were not receiving the best allocation. PARAMEDIC guarded against this by including all eligible cardiac arrests that were attended by trial vehicles. It was not clear whether this was also the case in ASPIRE. Second, the threshold for initiating a resuscitation attempt could have varied according to the intervention. For example, if a crew believed strongly that mechanical chest compression was better, they might initiate a resuscitation attempt in a situation where they would not if manual chest compression was to be used. In PARAMEDIC, the Data Monitoring Committee reviewed evidence for differential thresholds for resuscitation, but did not find evidence of any appreciable selection bias.

The ASPIRE trial found unfavourable results for survival and neurological outcome, and it was suggested that these effects were largely due to heterogeneity of treatment effects between sites. A re-analysis²⁰ of the trial, by researchers associated with the device manufacturers, found that the unfavourable outcomes may have been due to one trial site (of five), where the protocol was changed part-way through the study, resulting in a delay in the start of mechanical chest, which could have led to worse outcomes. However, the study investigators disagreed with this interpretation.²¹

The use of the double triangular test design in the CIRC trial raises a number of issues. The adjustment of the final analysis to allow for the interim analyses had a large effect on the primary outcome (survival to hospital discharge), changing the point estimate of the odds ratio from 0.89 to 1.06. The secondary analyses were not adjusted for the interim analyses, so the results for the primary and secondary outcomes were not directly comparable. Additionally, the boundaries for equivalence in the double triangular test were very generous; if the “equivalence” boundary were crossed, the 95% confidence interval would be contained between log-odds of -0.37 and 0.37 (i.e. odds ratio of 0.69 and 1.45).¹⁵ This interval includes values that would represent substantial benefit and substantial harm, so the conclusion of “equivalence” in this situation is questionable.

In some trials, a high proportion of survivors had missing data for neurologically intact survival. This was most severe in CIRC, where 27.7% of survivors lacked data for this outcome. This reflects the difficulty of performing follow-up assessments on cardiac arrest survivors, but clearly has the potential to introduce bias. It is possible, or even likely, that there could be an association between missingness and neurological outcome. There are many plausible reasons why patients with poor outcomes may be more likely to be lost, for example, they may be harder to contact because they have moved to a residential care facility, or they may be less willing or able to undertake follow-up assessments.

Non-compliance was a major issue in PARAMEDIC, where 40% of the mechanical chest compression group actually received this intervention. It was designed as a pragmatic trial, so some non-compliance, which would occur in normal clinical practice, was anticipated. This would include cases where the patients was too large or too small for LUCAS, the LUCAS could not be deployed due to space restrictions, or where the original call was not for cardiac arrest, and the arrest occurred while the patient was being treated by a solo responder. The PARAMEDIC investigators also carried out CACE analyses to assess the treatment effects of LUCAS when it was actually used. These analyses confirmed the overall analyses: the treatment effects were similar when LUCAS was actually used, providing evidence that the non-compliance was not causing failure to find a treatment benefit.

Quality of CPR provided in the manual chest compression arms of the trials could affect the results; if manual chest compression was high quality, mechanical devices may not appear superior, as one of their main benefits is to provide consistent chest compressions over long periods, which is known to be difficult for humans. Measuring the quality of CPR in a large trial is very challenging, but several of the trials did provide some information. In CIRC, CPR quality data were collected from 96% of participants, and showed compression fractions in the first 5 min of 79.0% (sd 12.3%) in the manual group and 74.7% (sd 12.7%) in the mechanical arm. The target compression rates in the two arms of this trial were different: 100/min in the manual arm and 80/min in the mechanical arm. The target was achieved more often in the manual arm: median compression rate in the manual arm was 89.9 (IQR 79.3, 100.3), but in the mechanical arm it was 65.9 (IQR 61.3, 70.2). In LINC compression fraction was recorded from 10% of patients, and was 84% in the mechanical compression group and 78% in the manual group. ASPIRE recorded compression fraction in the first 5 min from 45% of the manual compression group and 52% of the mechanical compression group; it was very similar, at 0.6 (sd 0.2) in the manual arm and 0.59 (sd 0.21) in the mechanical arm. The remaining two trials did not report any information on CPR quality.

5. Conclusion

Meta-analyses of the results from randomised controlled which enrolled over 10,000 patients do not suggest that mechanical chest compression devices are superior to manual chest compression, when used routinely during resuscitation after out of hospital cardiac arrest. The widespread deployment of devices based on clinical effectiveness does not seem justified. Nevertheless, it is likely that mechanical chest compression devices will continue to play a role in resuscitation. Mechanical devices can deliver chest compressions where manual CPR is difficult or impossible, such as during ambulance transport, and are likely to be the best treatment option in such situations. The use of mechanical devices for in-hospital cardiac arrest has not been evaluated in randomised trials, but the results for prehospital studies may not extrapolate to this setting. Mechanical devices may also be used as a bridge to advanced treatments such as extracorporeal membrane oxygenation.⁶

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Conflict of interest statement

S.G. and G.D.P. were Co-Chief Investigators for PARAMEDIC. T.Q., C.D.D. and L.B. were involved in running the PARAMEDIC trial. K.C. has no conflicts of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.resuscitation.2015.07.002>

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